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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/762,873
Filing Date: January 21, 2004
Appellant(s): VALIANTE, NICHOLAS M.

Leslie A. Robinson
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/28/10 appealing from the Office action mailed 10/6/08.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of the claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

Baker et al. (US Patent 5,441,955)

Colston et al. (US Patent 7,122,195 B2)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 12-17, 19 are rejected under 35 U.S.C. 103(a) as being obvious over Baker et al. (US Patent 5,441,955) in view of Colston et al. (US Patent 7,122,195 B2).

The instant claims are directed to a composition comprising a tryptanthrin compound (No. 1001) and an antigen.

Baker et al. teach the tryptanthrin compound of No. 1001 in the applicant's specification (col. 20, lines 22-33) as part of an antimicrobial composition (abstract).

Furthermore, this tryptanthrin compound can be administered with an adjuvant (col. 12, lines 37-42). What's more, Baker et al. teach that tryptanthrin can be administered in combination with one or more other agents used in the treatment of pathogenic mycobacterial infections. Representative agents used for the treatment of mycobacterial tuberculosis include, for example, isoniazid, rifampin, pyrazinamide, ethambutol, rifabutin, streptomycin, and ciproflaxin (col. 13, lines 35-43). Examiner would like to point out that mycobacterial tuberculosis is a common cause of bacterial meningitis (meningococcus infection). Moreover, Bacillus of Calmette and Guérin (BCG) is a vaccine against tuberculosis caused by mycobacterial tuberculosis.

Examiner reminds Applicant that the limitation "for enhancing an immune response" in claim 12 is considered preamble or intended use, since the claims are drawn to a composition, therefore will given little patentable weight.

It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish from each other. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Thus, the intended use of a composition claim will be given no patentable weight.

It is further respectfully pointed out that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use

of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See MPEP 2111.02.

Examiner further reminds Applicant that the limitations "immunogenic" and "providing an enhanced immune response to the antigen than provided without the tryptanthrin compound adjuvant" in claim 12 as well as "enhances an immune response to the antigen and the immune response is the cellular production of one or more cytokines" in claim 15 will be given little patentable weight since a composition and its properties are inseparable.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

Baker et al., however fails to disclose a specific combination of the tryptanthrin compound (No. 1001) and an antigen disclosed in claim 14.

Colston et al. teach that recA mutant mycobacteria, particularly mutants of mycobacterial species which are members of Mycobacterium tuberculosis, are useful as

vaccines for the treatment of a range of disorders, including tuberculosis (abstract). Colston et al. teach that this invention may be used as an antigen delivery system in the treatment of any disease, such as pathogenic infection, which is ameliorated by an immune response against a particular antigen. Suitable antigens include viral, protozoal, tumour cell, bacterial, and fungal antigens, for example an antigen from the Tetanustoxin, and Diphtheriatoxin. Such an antigen may be useful in the treatment of tetanus and diphtheria (col. 4, line 51 to col. 5, line 14).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to combine the tryptanthrin compound (No. 1001) as disclosed by Baker et al. with the composition comprising antigens associated with tetanus or diphtheria as disclosed by Colston et al.

A person of ordinary skill in the art would have been motivated to combine the tryptanthrin compound (No. 1001) with a composition comprising antigens associated with tetanus or diphtheria because: (1) both Baker and Colston are analogous are since both teach the treatment of pathogenic mycobacterial infections, for example tuberculosis; (2) Baker teaches that the tryptanthrin compound can be administered with an adjuvant or another agent used in the treatment of pathogenic mycobacterial infections; (3) Baker teaches the use of antigens such as BCG in a vaccine against tuberculosis; (4) Colston teaches an antigen delivery system in the treatment of any disease, such as pathogenic infection, which is ameliorated by an immune response against a particular antigen; and (5) Colston specifically discloses suitable antigens,

such as include viral, protozoal, tumour cell, bacterial, and fungal antigens, for example antigens from the Tetanustoxin and Diphtheriatoxin.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

(10) Response to Argument

Appellant argues nonobviousness because the rejection requires mixing a vaccine composition that requires a live mycobacterium for its effectiveness with a tryptanthrin compound that is disclosed to kill mycobacteria. The Office has failed to provide a rationale sufficient to motivate one of ordinary skill in the art to combine the disclosures of Baker and Colston in view of this fundamental incompatibility between the cited references. One would expect that the combination of the antibacterial of Baker and the vaccine of Colston would be expected to be ineffective, since the antibacterial compound would be expected to kill the vaccine's active cells. Thus it would not be logical to administer BCG along with an antibacterial like the compounds of Formula I because the antibacterial would be expected to harm the bacteria in the vaccine or in the treated patient.

This is not persuasive because Appellant is arguing against their own claimed invention. If the composition comprising the combination of the cited prior art is ineffective, why is it that the same composition claimed by the Appellant be enabled?

Appellant argues against Examiner's response by stating that the claimed compositions do not include a live mycobacterium cell, and such cell is not required to provide an enhanced immune response to the antigen in the claimed compositions because the tryptanthrin compound itself functions as an adjuvant.

This is not persuasive because Appellant has not mentioned the fact that the vaccines encompassed by the claims may include live viral and bacterial immunogens as taught by the instant specification (paragraphs 0111-0121). Considering the claimed invention can also potentially include live bacteria, why is it that only in the composition taught by the prior art would be inactivated by tryptanthrin? It is improper to argue that something will happen in one composition and not in another composition when the two are the same. Further, Appellant has not provided any factual evidence that tryptanthrin would indeed render the vaccine ineffective. Furthermore, even if the viral or bacteria immunogen would be killed, it matters little since most vaccines use completely killed or attenuated (weakened) immunogens. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success.

Appellant argues against using Kerkhoven case law because this case is an entirely different situation. The compositions in this case are not merely two conventional cleaning agents that one might casually mix together. Here, one of the compositions is an antibacterial compound, which acts by killing a bacterium, according to Baker. The other is a vaccine composition that acts by a completely different mechanism, eliciting an immune response. Thus, the two materials require different

formulations, different administration schedules, and different storage conditions as well as have different effects, purposes, and are suitable for use in different patients.

This is not persuasive because while these differences may or may not be true, the fact remains that Baker discloses these two active agents for the treatment of pathogenic mycobacterial infections. Baker also teaches that tryptanthrin can be administered in combination with one or more agents or adjuvants. Appellant is also reminded that there are many combination therapies in the medical field that work via different or multiple mechanisms of action. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating pathogenic mycobacterial infections by administering tryptanthrin with an adjuvant because of the therapeutically additive effect of combining two known active agents for the same purpose.

Appellant argues that even if a compound of Baker was for some reason physically admixed with a vaccine composition, nothing in the cited art would lead one of skill in the art to conclude that the tryptanthrin compound would necessarily be present in an amount effective to promote an enhanced immune response to an antigen, as required by the claims.

This is not persuasive because the instant claims do not recite a particular dosage range that will enable the tryptanthrin compound to promote an enhanced immune response to an antigen. Therefore, interpreting the claim broadly, any dosage amount of tryptanthrin will obviously have the same properties.

Furthermore, the specification is not clear on what the metes and bounds are regarding the dosage amount of tryptanthrin to promote an enhanced immune response to an antigen. Paragraph 103 on page 25 merely provides a preferred embodiment of this dosage amount. Paragraph 141 on page 39 states that the compounds of this invention and other therapeutically active agents can be administered at the recommended maximum clinical dosage or at lower dosages. Dosage levels are varied depending upon various factors. The guidance of the specification is limited to this, as it does not contain a clear teaching of the tryptanthrin dosage that is needed to promote an enhanced immune response to an antigen.

Examiner notes that the Baker reference clearly teaches the administration of tryptanthrin. Baker teaches the total daily dose to be from 0.001 to 1000 mg/kg body weight. It is understood that the specific dose level for any particular patient will depend upon a variety of factors including the activity of the specific compound, age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination, and the severity of the particular disease (col. 12, lines 20-36). Should the Appellant continue to argue this issue, Examiner encourages Appellant to show factual evidence that the particular dosage range of tryptanthrin taught by Baker would not obviously promote an enhanced immune response to an antigen.

Appellant argues that since drug interactions are common, one does not casually combine drugs merely because they are known in a general sense to be useful for treating a particular type of condition. Appellant submits Exhibit A to show that the user of BCG is specifically advised to tell her doctor if she is using antibiotics, which

suggests that drug interactions with antibiotics are a concern for a user of BCG. Appellant also argues that it would not be obvious to combine the two into a single composition because vaccines are typically administered once, whereas antibacterials are typically administered over a period of days and in many doses.

This is not persuasive because this line of reasoning is applicable to any combination of drugs. Naturally, this is a general concern for anyone in the medical field, however nothing in Exhibit A states that BCG cannot be combined with another active agent, let alone a compound of Formula I. In fact, nothing is even said about drug to drug interactions in Exhibit A. Furthermore, Appellant's arguments directed to the number of doses are not persuasive because even a single dose of an antibacterial compound along with a single vaccine would be enough to render the claimed composition obvious. In other words, there is nothing in the claims to preclude the further administration of the same antibacterial minus the vaccine since the claims use the open transitional language "comprising."

In regards to Exhibit B, the reference does not state that the combination of vaccines and antibiotics will not work, but that the combination will be less effective. Nonetheless, the reference says nothing about the particular combination cited by the prior art or the claimed invention. Appellant is reminded that the standard for obviousness is not absolute but a reasonable expectation of success.

Appellant argues that the prior art does not disclose the claimed composition, therefore the claimed properties are not present in the prior art. The compounds of Formula I were at least partially known because they were not known to be mixed with

an antigen. Therefore, the limitation "to provide an enhanced immune response to the antigen relative to the response provided without the tryptanthrin compound adjuvant" should be afforded patentable weight. This phrase limits the composition in a substantive way, though it does so using a functional limitation.

This is not persuasive because the claimed composition is disclosed by the cited prior art. Appellant is reminded that the obviousness rejection is based on the combination of two prior art references, which must be considered together. In response to appellant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on the combination of references. See *In re Keller*, 642 F. 2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Since the cited prior art discloses all components in the prior art, the limitations drawn to the properties of the composition is inherent. Appellant is invited to show factual data showing that the composition rendered obvious by the cited prior art does not possess the same functional properties of the claimed composition.

Appellant argues against a case of obviousness by claiming unexpected results in the form of the immunogenic effect of an antigen as enhanced by a compound of Formula I.

The Valiante Declaration under 37 CFR 1.132 filed 10/31/2007 is insufficient to overcome the rejection of claims 12-17, 19 based upon Baker et al. (US Patent 5,441,955) in view of Colston et al. (US Patent 7,122,195 B2).

It include(s) statements which amount to an affirmation that the claimed subject matter functions as it was intended to function. This is not relevant to the issue of nonobviousness of the claimed subject matter and provides no objective evidence thereof. See MPEP § 716.

The Valiante Declaration simply states that the tryptanthrin compound can be effective in generating an immune response as viewed in Table 1. The ability to stimulate TNF-alpha production is viewed as unexpected based on previously known properties of tryptanthrin. Examiner does not view this as unexpected properties since tryptanthrin is a known compound. Furthermore, the claims and rejection are based on the combination of tryptanthrin compound and an antigen in claim 14. There is no factual data, commensurate with the scope of the claims to overcome a prima facie case of obviousness.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Yong S. Chong/

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3/30/2010

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